

#2



OIPE

1582  
03/12  
ENTEREDRAW SEQUENCE LISTING  
PATENT APPLICATION: US/10/085,476DATE: 03/12/2002  
TIME: 15:11:01Input Set : A:\IT0002PCA.TXT  
Output Set: N:\CRF3\03122002\J085476.raw

4 <110> APPLICANT: De Francesco, Raffaele  
 5 Tomei, Licia  
 6 Behrens, Sven-Erik  
 8 <120> TITLE OF INVENTION: METHOD FOR REPRODUCING IN VITRO THE  
 9 RNA-DEPENDENT RNA POLYMERASE AND TERMINAL NUCLEOTIDYL  
 10 TRANSFERASE ACTIVITIES ENCODED BY HEPATITIS C VIRUS (HCV)  
 13 <130> FILE REFERENCE: IT0002PCA  
 C--> 15 <140> CURRENT APPLICATION NUMBER: US/10/085,476  
 C--> 15 <141> CURRENT FILING DATE: 2002-02-27  
 15 <150> PRIOR APPLICATION NUMBER: 08/952,981  
 16 <151> PRIOR FILING DATE: 1998-03-23  
 18 <150> PRIOR APPLICATION NUMBER: PCT/IT96/00106  
 19 <151> PRIOR FILING DATE: 1996-05-24  
 21 <150> PRIOR APPLICATION NUMBER: RM95A000343  
 22 <151> PRIOR FILING DATE: 1995-05-25  
 24 <160> NUMBER OF SEQ ID NOS: 14  
 26 <170> SOFTWARE: FastSEQ for Windows Version 4.0  
 28 <210> SEQ ID NO: 1  
 29 <211> LENGTH: 591  
 30 <212> TYPE: PRT  
 31 <213> ORGANISM: Hepatitis C virus  
 33 <400> SEQUENCE: 1  
 34 Ser Met Ser Tyr Thr Trp Thr Gly Ala Leu Ile Thr Pro Cys Ala Ala  
 35 1 5 10 15  
 36 Glu Glu Ser Lys Leu Pro Ile Asn Ala Leu Ser Asn Ser Leu Leu Arg  
 37 20 25 30  
 38 His His Asn Met Val Tyr Ala Thr Thr Ser Arg Ser Ala Gly Leu Arg  
 39 35 40 45  
 40 Gln Lys Lys Val Thr Phe Asp Arg Leu Gln Val Leu Asp Asp His Tyr  
 41 50 55 60  
 42 Arg Asp Val Leu Lys Glu Met Lys Ala Lys Ala Ser Thr Val Lys Ala  
 43 65 70 75 80  
 44 Lys Leu Leu Ser Val Glu Glu Ala Cys Lys Leu Thr Pro Pro His Ser  
 45 85 90 95  
 46 Ala Lys Ser Lys Phe Gly Tyr Gly Ala Lys Asp Val Arg Asn Leu Ser  
 47 100 105 110  
 48 Ser Lys Ala Val Asn His Ile His Ser Val Trp Lys Asp Leu Leu Glu  
 49 115 120 125  
 50 Asp Thr Val Thr Pro Ile Asp Thr Thr Ile Met Ala Lys Asn Glu Val  
 51 130 135 140  
 52 Phe Cys Val Gln Pro Glu Lys Gly Gly Arg Lys Pro Ala Arg Leu Ile  
 53 145 150 155 160  
 54 Val Phe Pro Asp Leu Gly Val Arg Val Cys Glu Lys Met Ala Leu Tyr

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55	165	170	175
56	Asp Val Val Ser Thr Leu Pro Gln Val Val Met Gly Ser Ser Tyr Gly		
57	180	185	190
58	Phe Gln Tyr Ser Pro Gly Gln Arg Val Glu Phe Leu Val Asn Thr Trp		
59	195	200	205
60	Lys Ser Lys Lys Asn Pro Met Gly Phe Ser Tyr Asp Thr Arg Cys Phe		
61	210	215	220
62	Asp Ser Thr Val Thr Glu Asn Asp Ile Arg Val Glu Glu Ser Ile Tyr		
63	225	230	235
64	240	245	255
65	Gln Cys Cys Asp Leu Ala Pro Glu Ala Arg Gln Ala Ile Lys Ser Leu		
66	260	265	270
67	Thr Glu Arg Leu Tyr Ile Gly Gly Pro Leu Thr Asn Ser Lys Gly Gln		
68	275	280	285
69	Asn Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Thr Thr Ser		
70	290	295	300
71	Cys Gly Asn Thr Leu Thr Cys Tyr Leu Lys Ala Ser Ala Ala Cys Arg		
72	305	310	315
73	Ala Ala Lys Leu Gln Asp Cys Thr Met Leu Val Asn Gly Asp Asp Leu		
74	320	325	330
75	Val Val Ile Cys Glu Ser Ala Gly Thr Gln Glu Asp Ala Ala Ser Leu		
76	335	340	345
77	Arg Val Phe Thr Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro Gly Asp		
78	350	355	360
79	Pro Pro Gln Pro Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys Ser Ser		
80	365	370	375
81	Asn Val Ser Val Ala His Asp Ala Ser Gly Lys Arg Val Tyr Tyr Leu		
82	380	385	390
83	Thr Arg Asp Pro Thr Thr Pro Leu Ala Arg Ala Ala Trp Glu Thr Ala		
84	400	405	410
85	Arg His Thr Pro Val Asn Ser Trp Leu Gly Asn Ile Ile Met Tyr Ala		
86	415	420	425
87	Pro Thr Leu Trp Ala Arg Met Ile Leu Met Thr His Phe Phe Ser Ile		
88	430	435	440
89	Leu Leu Ala Gln Glu Gln Leu Glu Lys Ala Leu Asp Cys Gln Ile Tyr		
90	445	450	455
91	Gly Ala Cys Tyr Ser Ile Glu Pro Leu Asp Leu Pro Gln Ile Ile Glu		
92	460	465	470
93	Arg Leu His Gly Leu Ser Ala Phe Ser Leu His Ser Tyr Ser Pro Gly		
94	480	485	490
95	Glu Ile Asn Arg Val Ala Ser Cys Leu Arg Lys Leu Gly Val Pro Pro		
96	495	500	505
97	Leu Arg Val Trp Arg His Arg Ala Arg Ser Val Arg Ala Arg Leu Leu		
98	510	515	520
99	Ser Gln Gly Gly Arg Ala Ala Thr Cys Gly Lys Tyr Leu Phe Asn Trp		
100	525	530	535
101	Ala Val Lys Thr Lys Leu Lys Leu Thr Pro Ile Pro Ala Ala Ser Arg		
102	540	545	550
103	Leu Asp Leu Ser Gly Trp Phe Val Ala Gly Tyr Ser Gly Gly Asp Ile		
	555	560	

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104 Tyr His Ser Leu Ser Arg Ala Arg Pro Arg Trp Phe Met Leu Cys Leu  
105 565 570 575  
106 Leu Leu Leu Ser Val Gly Val Gly Ile Tyr Leu Leu Pro Asn Arg  
107 580 585 590  
109 <210> SEQ ID NO: 2  
110 <211> LENGTH: 2201  
111 <212> TYPE: PRT  
112 <213> ORGANISM: cDNA clone pCD (38-9.4)  
114 <400> SEQUENCE: 2  
115 Met Asp Arg Glu Met Ala Ala Ser Cys Gly Gly Ala Val Phe Val Gly  
116 1 5 10 15  
117 Leu Val Leu Leu Thr Leu Ser Pro Tyr Tyr Lys Val Phe Leu Ala Arg  
118 20 25 30  
119 Leu Ile Trp Trp Leu Gln Tyr Phe Thr Thr Arg Ala Glu Ala Asp Leu  
120 35 40 45  
121 His Val Trp Ile Pro Pro Leu Asn Ala Arg Gly Arg Asp Ala Ile  
122 50 55 60  
123 Ile Leu Leu Met Cys Ala Val His Pro Glu Leu Ile Phe Asp Ile Thr  
124 65 70 75 80  
125 Lys Leu Leu Ile Ala Ile Leu Gly Pro Leu Met Val Leu Gln Ala Gly  
126 85 90 95  
127 Ile Thr Arg Val Pro Tyr Phe Val Arg Ala Gln Gly Leu Ile His Ala  
128 100 105 110  
129 Cys Met Leu Val Arg Lys Val Ala Gly Gly His Tyr Val Gln Met Ala  
130 115 120 125  
131 Phe Met Lys Leu Gly Ala Leu Thr Gly Thr Tyr Ile Tyr Asn His Leu  
132 130 135 140  
133 Thr Pro Leu Arg Asp Trp Pro Arg Ala Gly Leu Arg Asp Leu Ala Val  
134 145 150 155 160  
135 Ala Val Glu Pro Val Val Phe Ser Asp Met Glu Thr Lys Ile Ile Thr  
136 165 170 175  
137 Trp Gly Ala Asp Thr Ala Ala Cys Gly Asp Ile Ile Leu Gly Leu Pro  
138 180 185 190  
139 Val Ser Ala Arg Arg Gly Lys Glu Ile Leu Leu Gly Pro Ala Asp Ser  
140 195 200 205  
141 Leu Glu Gly Arg Gly Leu Arg Leu Leu Ala Pro Ile Thr Ala Tyr Ser  
142 210 215 220  
143 Gln Gln Thr Arg Gly Leu Leu Gly Cys Ile Ile Thr Ser Leu Thr Gly  
144 225 230 235 240  
145 Arg Asp Lys Asn Gln Val Glu Gly Glu Val Gln Val Val Ser Thr Ala  
146 245 250 255  
147 Thr Gln Ser Phe Leu Ala Thr Cys Val Asn Gly Val Cys Trp Thr Val  
148 260 265 270  
149 Tyr His Gly Ala Gly Ser Lys Thr Leu Ala Ala Pro Lys Gly Pro Ile  
150 275 280 285  
151 Thr Gln Met Tyr Thr Asn Val Asp Gln Asp Leu Val Gly Trp Pro Lys  
152 290 295 300  
153 Pro Pro Gly Ala Arg Ser Leu Thr Pro Cys Thr Cys Gly Ser Ser Asp  
154 305 310 315 320

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155 Leu Tyr Leu Val Thr Arg His Ala Asp Val Ile Pro Val Arg Arg Arg  
 156 325 330 335  
 157 Gly Asp Ser Arg Gly Ser Leu Leu Ser Pro Arg Pro Val Ser Tyr Leu  
 158 340 345 350  
 159 Lys Gly Ser Ser Gly Gly Pro Leu Leu Cys Pro Phe Gly His Ala Val  
 160 355 360 365  
 161 Gly Ile Phe Arg Ala Ala Val Cys Thr Arg Gly Val Ala Lys Ala Val  
 162 370 375 380  
 163 Asp Phe Val Pro Val Glu Ser Met Glu Thr Thr Met Arg Ser Pro Val  
 164 385 390 395 400  
 165 Phe Thr Asp Asn Ser Ser Pro Pro Ala Val Pro Gln Ser Phe Gln Val  
 166 405 410 415  
 167 Ala His Leu His Ala Pro Thr Gly Ser Gly Lys Ser Thr Lys Val Pro  
 168 420 425 430  
 169 Ala Ala Tyr Ala Ala Gln Gly Tyr Lys Val Leu Val Leu Asn Pro Ser  
 170 435 440 445  
 171 Val Ala Ala Thr Leu Gly Phe Gly Ala Tyr Met Ser Lys Ala His Gly  
 172 450 455 460  
 173 Ile Asp Pro Asn Ile Arg Thr Gly Val Arg Thr Ile Thr Thr Gly Ala  
 174 465 470 475 480  
 175 Pro Val Thr Tyr Ser Thr Tyr Gly Lys Phe Leu Ala Asp Gly Gly Cys  
 176 485 490 495  
 177 Ser Gly Gly Ala Tyr Asp Ile Ile Cys Asp Glu Cys His Ser Thr  
 178 500 505 510  
 179 Asp Ser Thr Thr Ile Leu Gly Ile Gly Thr Val Leu Asp Gln Ala Glu  
 180 515 520 525  
 181 Thr Ala Gly Ala Arg Leu Val Val Leu Ala Thr Ala Thr Pro Pro Gly  
 182 530 535 540  
 183 Ser Val Thr Val Pro His Pro Asn Ile Glu Glu Val Ala Leu Ser Asn  
 184 545 550 555 560  
 185 Thr Gly Glu Ile Pro Phe Tyr Gly Lys Ala Ile Pro Ile Glu Ala Ile  
 186 565 570 575  
 187 Arg Gly Gly Arg His Leu Ile Phe Cys His Ser Lys Lys Lys Cys Asp  
 188 580 585 590  
 189 Glu Leu Ala Ala Lys Leu Ser Gly Leu Gly Ile Asn Ala Val Ala Tyr  
 190 595 600 605  
 191 Tyr Arg Gly Leu Asp Val Ser Val Ile Pro Thr Ile Gly Asp Val Val  
 192 610 615 620  
 193 Val Val Ala Thr Asp Ala Leu Met Thr Gly Tyr Thr Gly Asp Phe Asp  
 194 625 630 635 640  
 195 Ser Val Ile Asp Cys Asn Thr Cys Val Thr Gln Thr Val Asp Phe Ser  
 196 645 650 655  
 197 Leu Asp Pro Thr Phe Thr Ile Glu Thr Thr Val Pro Gln Asp Ala  
 198 660 665 670  
 199 Val Ser Arg Ser Gln Arg Arg Gly Arg Thr Gly Arg Gly Arg Arg Gly  
 200 675 680 685  
 201 Ile Tyr Arg Phe Val Thr Pro Gly Glu Arg Pro Ser Gly Met Phe Asp  
 202 690 695 700  
 203 Ser Ser Val Leu Cys Glu Cys Tyr Asp Ala Gly Cys Ala Trp Tyr Glu

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Input Set : A:\IT0002PCA.TXT  
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204	705	710	715	720
205	Leu Thr Pro Ala Glu Thr Ser Val Arg Leu Arg Ala Tyr Leu Asn Thr			
206	725	730	735	
207	Pro Gly Leu Pro Val Cys Gln Asp His Leu Glu Phe Trp Glu Ser Val			
208	740	745	750	
209	Phe Thr Gly Leu Thr His Ile Asp Ala His Phe Leu Ser Gln Thr Lys			
210	755	760	765	
211	Gln Ala Gly Asp Asn Phe Pro Tyr Leu Val Ala Tyr Gln Ala Thr Val			
212	770	775	780	
213	Cys Ala Arg Ala Gln Ala Pro Pro Pro Ser Trp Asp Gln Met Trp Lys			
214	785	790	795	800
215	Cys Leu Ile Arg Leu Lys Pro Thr Leu His Gly Pro Thr Pro Leu Leu			
216	805	810	815	
217	Tyr Arg Leu Gly Ala Val Gln Asn Glu Val Thr Leu Thr His Pro Ile			
218	820	825	830	
219	Thr Lys Tyr Ile Met Ala Cys Met Ser Ala Asp Leu Glu Val Val Thr			
220	835	840	845	
221	Ser Thr Trp Val Leu Val Gly Gly Val Leu Ala Ala Leu Ala Ala Tyr			
222	850	855	860	
223	Cys Leu Thr Thr Gly Ser Val Val Ile Val Gly Arg Ile Ile Leu Ser			
224	865	870	875	880
225	Gly Arg Pro Ala Ile Val Pro Asp Arg Glu Leu Leu Tyr Gln Glu Phe			
226	885	890	895	
227	Asp Glu Met Glu Glu Cys Ala Ser His Leu Pro Tyr Ile Glu Gln Gly			
228	900	905	910	
229	Met Gln Leu Ala Glu Gln Phe Lys Gln Lys Ala Leu Gly Leu Leu Gln			
230	915	920	925	
231	Thr Ala Thr Lys Gln Ala Glu Ala Ala Ala Pro Val Val Glu Ser Lys			
232	930	935	940	
233	Trp Arg Ala Leu Glu Thr Phe Trp Ala Lys His Met Trp Asn Phe Ile			
234	945	950	955	960
235	Ser Gly Ile Gln Tyr Leu Ala Gly Leu Ser Thr Leu Pro Gly Asn Pro			
236	965	970	975	
237	Ala Ile Ala Ser Leu Met Ala Phe Thr Ala Ser Ile Thr Ser Pro Leu			
238	980	985	990	
239	Thr Thr Gln Ser Thr Leu Leu Phe Asn Ile Leu Gly Gly Trp Val Ala			
240	995	1000	1005	
241	Ala Gln Leu Ala Pro Pro Ser Ala Ala Ser Ala Phe Val Gly Ala Gly			
242	1010	1015	1020	
243	Ile Ala Gly Ala Ala Val Gly Ser Ile Gly Leu Gly Lys Val Leu Val			
244	1025	1030	1035	1040
245	Asp Ile Leu Ala Gly Tyr Gly Ala Gly Val Ala Gly Ala Leu Val Ala			
246	1045	1050	1055	
247	Phe Lys Val Met Ser Gly Glu Met Pro Ser Thr Glu Asp Leu Val Asn			
248	1060	1065	1070	
249	Leu Leu Pro Ala Ile Leu Ser Pro Gly Ala Leu Val Val Gly Val Val			
250	1075	1080	1085	
251	Cys Ala Ala Ile Leu Arg Arg His Val Gly Pro Gly Glu Gly Ala Val			
252	1090	1095	1100	

VERIFICATION SUMMARY  
PATENT APPLICATION: US/10/085,476

DATE: 03/12/2002  
TIME: 15:11:02

Input Set : A:\IT0002PCA.TXT  
Output Set: N:\CRF3\03122002\J085476.raw

L:15 M:270 C: Current Application Number differs, Replaced Current Application No  
L:15 M:271 C: Current Filing Date differs, Replaced Current Filing Date